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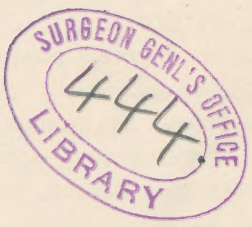

THE INFLUENCE OF ALCOHOL ON PROTEID METABOLISM.

By R. H. CHITTENDEN, *Professor of Physiological Chemistry in Yale University.*

(*From experiments made by* Messrs CHARLES NORRIS Jr. AND E. E. SMITH, *Assistant in Physiological Chemistry.*)

ALTHOUGH much work has been done with a view to ascertaining the influence of alcohol on nutrition, there is still great lack of unanimity of opinion as to its influence on the metabolism of proteid matter.

Many observers have reported a diminished excretion of nitrogen during the administration of alcohol, thus implying a diminution of proteid metabolism, while others have found the elimination of urea or nitrogen wholly unchanged. While there is a general impression that alcohol tends to lower the nitrogen output, or in other words to check the metabolism of proteid matter, and that wholly irrespective of the amount taken, the facts at our disposal are hardly sufficient to warrant such an assumption. As has been well pointed out by Warren[1] and Reichert[2] few, if any, of the old experiments have much value now. The older observers rarely went further than to determine the daily excretion of urea, wholly ignoring the residual nitrogen and the nitrogen of the fæces. Furthermore, the necessity of having the body in a condition of nitrogenous equilibrium, when studying the influence of a substance on nutrition, was not as fully appreciated then as at the present day.

Of the more recent experiments those made by Munk[3] appear to be the most trustworthy. This observer experimented with dogs of 18—20 kilos. body weight, in a condition of nitrogenous equilibrium, giving

[1] *Boston Med. and Surg. Journal*, July, 1887.

[2] "The action of alcohol on animal heat functions." *Therapeutic Gazette*, Feb. 1890.

[3] *Verhandl. d. Physiol. Gesellsch.* Berlin. Jan. 3, 1879. Also *Jahresbericht für Thierchemie für* 1878. p. 310.

alcohol in small or large doses for three to five days and comparing the excretion of nitrogen by the urine and fæces during this period with a like period in which no alcohol was given. The results appear to show that while smaller doses, 25 c.c. absolute alcohol, tend to diminish slightly the total nitrogen output, larger doses of 40—50 c.c. of absolute alcohol per day decidedly increase the elimination of nitrogen. In this connection it is to be remembered that v. Boeck and Bauer[1] found that with small doses of alcohol there was a diminished excretion of carbonic acid and inflow of oxygen, while larger doses led to an increased consumption of oxygen and excretion of carbonic acid. Hence, Munk concludes that in general, moderate doses of 1—1½ c.c. of absolute alcohol per kilo. lessen the decomposition of proteid matter to the extent of 6—7 per cent., while larger doses of 2 c.c. absolute alcohol per kilo. of body weight increase proteid metabolism 4 to 10 per cent. Munk also noticed that after giving large doses of alcohol, the further administration of small doses failed then to produce any diminution in the consumption of proteid matter, or only to a slight extent. Riess[2], on the other hand, experimenting with men and giving 3—5 grams of absolute alcohol per kilo. of body weight found both the urea and uric acid of the urine diminished 15—16 per cent. during an alcohol period of 13 days, thus implying diminished proteid metabolism, but the men experimented with were apparently not in nitrogenous equilibrium. Further, in experiments published last year, Keller[3], experimenting on himself and taking a single dose of 150 c.c. of 96 per cent. alcohol (2·4 c.c. per kilo. body weight), found a slight diminution in the nitrogen of the urine, but as the nitrogen of the fæces was not determined and there is no evidence that the body was in nitrogenous equilibrium this result is likewise of doubtful value.

With herbivora, Weiske has shown that small doses of alcohol (about 1 c.c. per kilo. body weight) exert no influence on proteid metabolism, when the animal receives his ordinary food. Further, Weiske and Flechsig[4] have found that much the same result is obtained when the animal is fed upon a very rich nitrogenous diet. Thus, in an experiment covering 32 days a sheep of 40 kilos. body weight took daily 60 grams of alcohol diluted to 1 litre, with food containing 22·24 grams of nitrogen. The total excretion of nitrogen

[1] *Zeitschrift für Biologie.* Band x. p. 336. 1870.
[2] *Zeitschrift für klin. Medicin.* 2. 1.
[3] *Zeitschrift für physiologische Chemie.* 1889. Band xiii. p. 128.
[4] *J. f. Landwirthschaft.* xxxvii. p. 327.

through the urine and fæces amounted during the fore period to 22·2 grams per day, while the daily output during the alcohol period was 22·4 grams, and in the after period 21·88 grams of nitrogen. Thus, from this experiment it would appear, that with herbivora, at least, alcohol does not protect the consumption of proteid matter like carbohydrates, but rather increases it.

It is plainly evident from these several results that we are not yet in a position to state definitely the action of alcohol upon proteid metabolism. Quite probably, as indicated by Munk's experiments, the action varies with variations in the conditions, but unfortunately many of the experiments hitherto tried have been lacking in some one respect to such an extent that the results need to be accepted with caution.

In the present study of the question, the experiments have been confined wholly to dogs, and in the administration of the alcohol we have followed Munk in the size of the doses, so that the conditions might be favourable for obtaining confirmation of his results.

The diet used throughout the experiments was a mixture of desiccated beef and milk crackers or biscuit. The meat was prepared by taking large quantities of lean beef (sufficient to last through an entire experiment), freeing it from fat and tendon, passing it through a hashing machine and then drying it at 45—50° C. until it had lost about 75 per cent. of its weight. The entire quantity was ground to a coarse powder, thoroughly mixed, and preserved in tightly closed jars. A sufficient amount of dry milk biscuit was likewise prepared by simply grinding it to a coarse powder. The percentages of nitrogen in both meat and biscuit were determined in sampled portions by the Kjeldahl method, thus giving us exact data on which to calculate the daily income of nitrogen.

First Experiment.

In this experiment, the dog used weighed a little over 16 kilos. He was confined in a suitable cage, lined with galvanized iron, adapted for the collection of the excreta. The meat employed as food contained 12·87 per cent. of nitrogen and the crackers or biscuit 1·81 per cent. of nitrogen. The daily rations consisted of 96 grams of the prepared beef and 80 grams of biscuit, mixed with 850 c.c. of water; one-half being given at 9 a.m., the other half at 5 p.m. The daily nitrogen income amounted therefore to 13·79 grams. The animal was confined in the cage and fed upon this diet for two weeks before the excretions were

analyzed, at the end of which time it was assumed that the animal had become habituated to the diet and his surroundings. The extent of nitrogenous metabolism was measured by daily determinations of the nitrogen of the urine, using the Kjeldahl method, and by determinations of total sulphur and phosphorus. The nitrogen of the fæces was likewise determined by Kjeldahl's method, whenever the animal defecated. Owing to the highly nutritive character of the food, however, this usually occurred only once in five days. Each day's urine represents the quantity excreted from 9 a.m. of one day to 9 a.m. of the following day, the date given in the tables being the day on which the 24 hours ended. Consequently, alcohol given on the 4th of April, for example, would have no effect on the urine of that date, but its influence would be looked for on the day following.

The method employed in the determination of total sulphur and phosphorus was to evaporate a given volume of the urine (50—100 c.c.) in a commodious silver crucible with pure potassium hydroxide and nitrate, igniting the residue until it was completely oxidized and treating the salts with water. For sulphur, the solution was acidified with hydrochloric acid, evaporated to dryness, the residue again dissolved, the solution filtered and precipitated after the usual method with barium chloride. For phosphorus, the solution was acidified with nitric acid, evaporated to dryness, the residue again dissolved and the solution precipitated first with molybdic solution and lastly with magnesia mixture. From the weight of magnesium pyrophosphate, the phosphorus was readily calculated.

The experiment extended through twenty-eight days and was divided into three periods; a fore or normal period of twelve days, during which no alcohol was given, an alcohol period of ten days during which 290 c.c. of absolute alcohol were administered, and lastly a short after period of six days. As seen from the table of results, the average daily output of nitrogen by the urine and fæces for the normal period amounted to 13·31 grams, while the daily income was 13·79 grams. The animal lost considerable hair which would account for a portion of the deficit in nitrogen, while the remainder must be attributed to the slight gain in body weight and in part to the ordinary losses in analytical work.

First Experiment.

Date	Body weight	Volume urine	Sp. gr.	Reaction	Nitrogen	Sulphur	Phosphorus	Absolute alcohol taken
March	kilos.	c.c.			grams	gram	gram	c.c.
24	16·1	810	1016	acid	12·973	0·862	0·609	0
25	16·1	800	1017	„	13·000	6·850	0·630	
26	16·2	850	1016	„	13·080	0·854	0·632	
27	16·1	820	1017	„	13·087	0·877	0·910	
28	16·3	745	1016	„	11·012	0·720	0·603	
29	16·2	780	1016	„	11·052	0·735	0·611	
30	16·3	955	1019	„	16·866	1·081	0·995	
31	16·2	860	1017	„	13·873	0·880	0·784	
April								
1	16·4	915	1016	„	13·993	0·881	0·822	
2	16·3	805	1017	„	13·600	0·897	0·762	
3	16·4	820	1017	„	13·567	0·874	0·778	
4	16·5	700	1014	„	9·267	0·699	0·496	10 10
Daily average		821	1016		12·947	0·850	0·719	

March 28. 113 gram fæces 2·510
April 3. 92 „ „ 1·890
Daily average nitrogen 13·314

Date	Body weight	Volume urine	Sp. gr.	Reaction	Nitrogen	Sulphur	Phosphorus	Absolute alcohol taken
April	kilos.	c.c.			grams	gram	gram	c.c.
5	16·2	820	1017	acid	12·511	0·721	0·682	15 15
6	16·3	850	1020	„	16·317	1·192	1·024	15 15
7	16·6	840	1016	„	12·602	0·879	0·763	15 15
8	16·8	850	1016	„	12·565	0·997	0·726	15 15
9	16·8	775	1016	„	12·632	0·732	0·795	15 15
10	16·7	800	1016	„	13·121	0·840	0·730	15 15
11	16·6	780	1017	„	13·322	0·860	0·736	15 15
12	16·8	810	1016	„	12·816	0·771	0·776	15 15
13	17·0	870	1016	„	13·278	0·853	0·772	15 15
14	16·8	740	1018	„	12·626	0·795	0·718	0
								Total alcohol
Daily average		813	1016		13·179	0·864	0·772	290

April 8. 96 grams fæces 2·020
„ 13. 98 „ „ 2·140
Daily average Nitrogen 13·595

Date	Body weight	Volume urine	Sp. gr.	Reaction	Nitrogen	Sulphur	Phosphorus	Absolute alcohol taken
April	kilos.	c.c.			grams	gram	gram	
15	16·8	800	1018	acid	13·108	0·810	0·790	0
16	16·8	830	1016	,,	13·161	0·820	0·793	
17	16·9	839	1017	,,	13·586	0·850	0·761	
18	16·8	831	1016	,,	13·749	0·889	0·762	
19	16·9	820	1017	,,	13·542	0·889	0·782	
20	17·0	735	1018	,,	10·982	0·686	0·639	
Daily average		809	1017		13·021	0·824	0·754	
April 20. 112 grams fæces					2·350			
Daily average Nitrogen					13·413			

During the alcohol period, in which 1·9 c.c. of absolute alcohol per kilo. of body weight were given daily for nine consecutive days, the average daily output of nitrogen amounted to 13·59 grams, an increase of about 2 per cent. over the average daily excretion of the normal period. The excretion of sulphur and phosphorus was likewise increased during the alcohol period to a corresponding extent. In the third or after period the excretion of all three elements fell back approximately to the normal.

The alcohol administered during the alcohol period was given in two distinct doses daily, mixed with the water of the food, and in no case did it apparently disagree with digestion. Unlike most previous experiments there was here no noticeable diuretic action, the average daily volume of urine being essentially the same during all three periods. The doses of alcohol were sufficiently large to produce drowsiness and a tendency towards stupor, the animal sleeping a great portion of the time during the alcohol period. There was further a slight weakness of the hind legs noticeable at times, particularly just after the doses of alcohol were given.

The results of this experiment may perhaps be taken as confirmatory of Munk's observations that fairly large doses of alcohol tend to increase somewhat the nitrogen output, thus implying increased metabolism of proteid matter. Our results certainly show a slightly increased excretion of nitrogen during the alcohol period, and this is confirmed by a corresponding increase in the excretion of sulphur and phosphorus. Considering, however, the size of the doses and the length of the alcohol period, it would seem as if a more decisive result might naturally be expected, if the substance experimented with is possessed of any very pronounced effect upon proteid metabolism.

Second Experiment.

In this experiment a somewhat smaller dog was employed, of about 13 kilos. body weight. The diet was of the same order as that made use of in the first experiment. The prepared meat contained 12·83 per cent. of nitrogen, as determined by the Kjeldahl method, and the biscuit 1·16 per cent. of nitrogen. The quantity of food given daily throughout the experiment consisted of 70 grams of prepared beef and 50 grams of milk biscuit with 500 c.c. of water. Hence the daily income of nitrogen amounted to 9·56 grams. This was fed to the animal at one time, instead of dividing it as in the first experiment, always at the same hour, viz. 10 a.m. Likewise, when the alcohol was given, the entire daily dose was mixed with the food and thus administered at one time.

In view of the possibility of alcohol exerting some special influence upon the elimination of either urea or uric acid, without necessarily affecting the excretion of total nitrogen, it was decided in this experiment to estimate not only the amount of nitrogen eliminated, but also the urea and uric acid. Phosphoric acid was also determined, but estimation of total sulphur and phosphorus was omitted. Uric acid was determined gravimetrically by E. Salkowski's well-known silver method[1]. Phosphoric acid by titration with a standard solution of uranyl nitrate. Urea, by titration with a standard solution of mercuric nitrate, after removal of the phosphates by baryta mixture and of chlorine by standard solution of silver nitrate. The standard mercury solution was prepared as recommended by Pflüger, and in the titration the acidity of the mixture was neutralized by a solution of sodium carbonate of 1053 specific gravity, after the method recommended by Pflüger. Total nitrogen in both the urine and fæces was determined by the Kjeldahl method.

The experiment was divided into three periods of ten days each. In the first or normal period, the average daily excretion of nitrogen through the urine and fæces amounted to 9·098 grams. This shows a deficit of 0·46 gram of nitrogen when compared with the daily nitrogen income; a deficiency due doubtless in part to loss of nitrogen by shedding of hair, and in part to the animal not being absolutely in nitrogenous equilibrium. The deficit, however, is not a large one and would mean at the most a laying up of 2·87 grams of proteid matter per day, or for the ten days' period of 28·7 grams proteid matter. In harmony with this, the animal appears to have gained slightly in weight.

[1] See Salkowski and Leube. *Die Lehre vom Harn.* pp. 96–97.

SECOND EXPERIMENT.

Date	Body wt.	Vol. urine	Sp. gr.	Nitrogen	Urea	Uric acid	Phosphoric acid (P_2O_5)	Nitrogen of fæces	Absolute alcohol taken
Jan.	kilos.	c.c.		grams	grams	gram	grams	grams	c.c.
13	12·6	530	1019	8·362	18·925	0·0402	1·109		
14	12·6	497	1018	8·771	17·940	0·0365	0·943		
15	12·8	475	1018	8·342	18·629	0·0377	1·216		
16	13·0	525	1016	7·824	16·851	0·0330	1·044		
17	12·9	615	1017	10·627	23·460	0·0286	1·494	0·558	
18	12·8	430	1023	8·916	18·542	0·0126	0·968	0·665	
19	12·9	510	1016	8·121	17·414	0·0339	1·204		
20	12·8	665	1017	10·829	22·512	0·0372	1·629		
21	12·8	420	1016	5·608	12·456	0·0271	0·871	1·773	
22	12·9	495	1021	10·586	22·359	0·0364	1·337		20·0
Total		5162		87·986	189·088	0·3232	11·815	2·996	
				2·996					
Total nitrogen, urine and fæces				90·982					

Date	Body wt.	Vol. urine	Sp. gr.	Nitrogen	Urea	Uric acid	Phosphoric acid (P_2O_5)	Nitrogen of fæces	Absolute alcohol taken
Jan.	kilos.	c.c.		grams	grams	gram	grams	grams	c.c.
23	12·8	585	1018	9·311	20·032	0·0570	1·257		25·6
24	12·9	480	1015	6·162	13·533	0·0480	0·955		25·8
25	12·9	470	1018	7·676	17·332	0·0277	1·014		25·8
26	13·0	550	1020	10·288	22·644	0·0690	1·304		26·0
27	13·0	535	1019	9·320	20·512	0·0570	1·205	0·280	32·5
28	13·0	575	1020	10·554	22·550	0·0449	1·473		32·5
29	13·1	450	1017	6·644	13·873	0·0277	0·992		32·8
30	13·1	550	1017	7·844	16·902	0·0358	1·099		39·3
31	13·0	550	1018	8·866	19·156	0·0393	1·249	1·572	39·0
Feb. 1	13·0	630	1019	10·843	22·679	0·0439	1·389		
Total		5375		87·508	189·213	0·4503	11·937	0·852	299·3
				1·852					
Total nitrogen, urine and fæces				89·360					

Date	Body wt.	Vol. urine	Sp. gr.	Nitrogen	Urea	Uric acid	Phosphoric acid (P_2O_5)	Nitrogen of fæces	Absolute alcohol taken
Feb.	kilos.	c.c.		grams	grams	gram	grams	grams	c.c.
2	13·0	650	1025	13·605	29·868	0·0487	1·817	0·075	0
3	13·0	520	1017	6·837	15·879	0·0216	1·117		
4	12·9	560	1021	10·341	21·416	0·0218	1·450		
5	12·9	540	1018	9·196	19·756	0·0219	1·322		
6	12·9	540	1017	9·072	18·860	0·0230	1·135		
7	12·9	500	1020	8·088	17·561	0·0230	1·238	0·917	
8	12·8	610	1019	10·710	22·376	0·0229	1·505		
9	12·6	570	1021	10·872	22·466	0·0316	1·460		
10	12·6	635	1018	9·705	19·948	0·0273	1·436	1·073	
11	12·7	525	1019	8·902	18·388	0·0297	1·276		
Total		5650		97·328	206·518	0·2715	13·756	2·065	
				2·065					
Total nitrogen, urine and fæces				99·393					

During the alcohol period of ten days, 299·3 cubic centimeters of absolute alcohol were given with a total excretion of 89·36 grams of nitrogen, as contrasted with the 90·98 grams of nitrogen of the normal period. This diminution in the excretion of nitrogen is very slight, and as it is accompanied by almost no change in the excretion of urea it cannot be considered as having any very decisive significance. The most noticeable result in the alcohol period is the decided increase in the elimination of uric acid. This commences immediately on the exhibition of the alcohol, continues throughout the alcohol period and the day following, and then suddenly drops to below the normal amount. The elimination of phosphoric acid during the alcohol period is not materially different from that of the fore period, neither is there any marked diuretic action under the influence of the alcohol. There is a slight increase in body weight.

In the after period, following the administration of alcohol, the total nitrogen output for the ten days amounts to 99·39 grams, which is a decided increase over the amount excreted during the fore period, and would at first glance indicate that the average daily excretion of nitrogen during the after period (9·93 grams) was greater than the daily income of nitrogen (9·56 grams). This, however, is not wholly true, for while the total nitrogen output in the after period is greater than the total nitrogen ingested, this is due to the very large amount of nitrogen eliminated on the first day of the after period, or the day following the

last dose of alcohol. Thus the average daily nitrogen output for the last nine days of the after period is 9·53 grams against 9·56 grams ingested. The body weight during the after period is seen to gradually fall back to that of the first few days of the fore period. In the light of the three periods of this series it seems fair to conclude that the alcohol has given rise to an increase in the excretion of uric acid and at the same time has diminished slightly the elimination of total nitrogen.

Third Experiment.

In this experiment the same animal was made use of as in the preceding one. The daily diet was changed slightly, the animal receiving 67 grams of prepared beef, 50 grams of sampled biscuit and 600 cubic centimeters of water. The meat used throughout the experiment contained 13·35 per cent. of nitrogen, the biscuit 0·58 per cent.; hence the animal received each day 9·52 grams of nitrogen. This experiment was somewhat shorter than the others, extending through twenty-four days, divided into three periods of eight days each.

In the fore or normal period, the total nitrogen income for the eight days amounted to 76·16 grams, while the total nitrogen output, through the urine and fæces amounted to 76·84 grams, thus showing a good condition of nitrogenous equilibrium. The body weight likewise remained constant.

THIRD EXPERIMENT.

Date	Body wt.	Vol. urine	Sp. gr.	Nitrogen	Urea	Uric acid	Phosphoric acid (P_2O_5)	Nitrogen of fæces	Absolute alcohol taken
Feb.	kilos.	c.c.		grams	grams	gram	grams	grams	c.c.
19	12·7	530	1019	9·528	19·915	0·0228	1·342		
20	12·6	690	1018	11·637	24·603	0·0210	1·489		
21	12·6	590	1017	9·141	19·667	0·0227	1·179		
22	12·6	495	1016	6·803	14·400	0·0208	1·021		
23	12·7	560	1019	9·944	21·382	0·0258	1·303		
24	12·5	590	1018	10·245	22·408	0·0271	1·367		
25	12·6	495	1018	8·637	18·681	0·0213	1·133		
26	12·6	530	1019	9·676	20·158	0·0209	1·337	1·232	31·5
Total		4480		75·611	161·214	0·1824	10·171	1·232	
				1·232					
Total nitrogen, urine and fæces				76·843					

Date	Body wt.	Vol. urine	Sp. gr.	Nitrogen	Urea	Uric acid	Phosphoric acid (P_2O_5)	Nitrogen of fæces	Absolute alcohol taken
Feb.	kilos.	c.c.		grams	grams	gram	grams	grams	c.c.
27	12·6	570	1016	8·118	17·646	0·0459	1·187		31·5
28	12·7	425	1017	6·635	14·285	0·0410	0·977		31·8
Mar.									
1	12·8	470	1018	7·857	16·675	0·0501	1·010		32·0
2	12·7	630	1020	12·271	25·819	0·0545	1·436	0·682	38·1
3	12·7	640	1018	9·915	21·008	0·0454	1·237		38·1
4	12·7	525	1016	7·448	15·840	0·0457	0·985		38·1
5	12·7	580	1017	8·719	19·039	0·0487	1·224		38·1
6	12·7	495	1018	8·221	17·368	0·0465	1·110	0·802	0
Total		4335		69·184	147·680	0·3778	9·166	1·484	279·2
				1·484					
Total nitrogen, urine and fæces				70·668					

Date	Body wt.	Vol. urine	Sp. gr.	Nitrogen	Urea	Uric acid	Phosphoric acid (P_2O_5)	Nitrogen of fæces	Absolute alcohol taken
Mar.	kilos.	c.c.		grams	grams	gram	grams	grams	c.c.
7	12·6	710	1024	14·387	29·656	0·0412	1·678		0
8	12·6	520	1019	8·293	17·631	0·0234	1·156		
9	12·6	625	1018	10·089	21·499	0·0384	1·413	1·033	
10	12·5	618	1019	10·436	22·655	0·0386	1·409		
11	12·6	470	1017	7·659	16·167	0·0310	1·115		
12	12·7	452	1016	6·678	14·837	0·0289	1·047		
13	12·7	575	1019	11·292	23·678	0·0405	1·462		
14	12·7	510	1020	10·378	21·402	0·0388	1·268	0·738	
Total		4480		79·212	167·575	0·2808	10·548	1·771	
				1·771					
Total nitrogen, urine and fæces				80·983					

During the alcohol period of eight days, 279·2 cubic centimeters of absolute alcohol were administered. The total amount of nitrogen eliminated during this period was 70·66 grams, being a decrease of over 6 grams in the eight days, or an average diminution of about three-fourths of a gram per day. The excretion of urea was correspondingly diminished during the alcohol period and likewise that of phosphoric acid. In conformity with this tendency towards diminished proteid metabolism there is to be noticed a slight increase in the body weight.

The most noticeable feature of the alcohol period, as in the last experiment, is the great increase in the excretion of uric acid. This increase commences on the first day following the exhibition of alcohol, and the average daily quantity eliminated amounts to more than double the quantity eliminated during the fore period. Further, in the after period, the amount excreted quickly drops to near the normal quantity.

Again, in the third or after period, the excretion of total nitrogen, urea and phosphoric acid rises to a little more than that of the normal period, indicating plainly that the animal was in good condition throughout the entire experiment, and that the action of the alcohol had unquestionably brought about an inhibition in the excretion of nitrogen, urea, etc., thus implying a diminution in the metabolism of proteid matter. In this connection it is to be observed that the total nitrogen income for the entire period of twenty-four days amounted to 228·48 grams, while the total nitrogen output for the same period, through the urine and fæces, amounted to 228·49 grams, thus showing an exceptionally close correspondence and giving us positive assurance of nitrogenous equilibrium. It is to be further observed that, as in the preceding experiment, the first day of the after period shows a very striking increase in the elimination of nitrogen, urea and phosphoric acid. This might naturally be interpreted as meaning that in the sudden withdrawal of the alcohol the check upon the metabolism of proteid matter was loosened, and consequently the production and excretion of these substances temporarily rose far above the normal amount.

In this experiment, as in the two preceding ones, there is no pronounced diuretic action noticeable.

Conclusions.

As a result of these three experiments we may conclude that alcohol, in the quantities employed by us, and in the case of dogs, has no very striking specific action upon the general metabolism of proteid matter. In this connection due weight must be attached to the length of the alcohol periods. In each case they extended through eight or ten days and under such conditions one would naturally expect a very pronounced result; one which would be independent of the minor fluctuations to be looked for in a shorter series, and which at the same time would be magnified by the length of the individual periods. Furthermore, the quantity of alcohol employed was large, rising to 2·5 cubic centimeters

of absolute alcohol per kilo. of body weight. Obviously, such a quantity given day after day should produce a decided result, if the substance is endowed with any special power to retard or stimulate tissue changes.

Our results lead us to the conclusion that alcohol, so far as its general influence on proteid metabolism is concerned, acts in the main simply as a non-nitrogenous food. As such it would yield a certain amount of energy by its own oxidation and thus tend to protect slightly the consumption of proteid matter and hence conserve the tissues. This view would accord with the recent results obtained by Reichert[1] in his study of the action of alcohol on animal heat functions. Assuming this view to be correct, one could not expect any very great diminution in the nitrogen output under the influence of alcohol; in fact, no greater than was observed in experiments 2 and 3, since it can save the tissues or the proteid food-stuff only to the extent of the energy which it can itself yield. At the same time it must be remembered that alcohol is a potent drug, and as such may exert at times some specific action upon metabolic changes. Possibly in this direction lies the explanation of the decided increase in the elimination of uric acid. Our results certainly indicate that alcohol has a decided and specific action in this direction, increasing the excretion of uric acid a hundred per cent, and that at a time when the elimination of urea and total nitrogen are being diminished.

Alcohol may then be considered as having the power to diminish somewhat the general metabolism of proteid matter, thus conserving the tissues; a power which is dependent mainly upon its character as a non-nitrogenous food. At the same time it has some specific action upon nutrition, as manifested in its tendency to increase the excretion of uric acid.

[1] *Therapeutic Gazette*, Feb. 1890.